

AMENDMENTS TO THE CLAIMS

The following listing of claims replaces all previous listing of claims.

1. (Withdrawn) A virus-like particle (VLP) comprising i) a fusion polypeptide comprising a polypeptide of interest (POI) and a particle-associating portion of an avian hepadnavirus large envelope polypeptide (L) or a functional derivative thereof and ii) an avian hepadnavirus small envelope (S) polypeptide or a functional derivative thereof.
2. (Withdrawn) The VLP of claim 1 comprising a fusion polypeptide comprising a polypeptide of interest (POI) and a particle-associating portion of a large envelope polypeptide (L) of duck hepatitis B virus (DHBV), or a functional derivative thereof.
3. (Withdrawn) The VLP of claim 1 or 2 comprising a fusion polypeptide comprising a polypeptide of interest (POI) and a particle-associating portion of a large envelope polypeptide (L) of duck hepatitis B virus (DHBV), or a functional derivative thereof and ii) a small envelope (S) polypeptide of DHBV, or a functional derivative thereof.
4. (Withdrawn) The VLP of claim 1 or 2 wherein the particle-associating portion of L comprises at least the S domain of L, or the S domain of L minus the TM1 domain, or a functional derivative thereof.
5. (Withdrawn) The VLP of claim 1 or 2 wherein the POI is located in the pre-S domain of L, or at the amino terminal side of the S domain of L, or the S domain minus the TM1 domain of L.
6. (Withdrawn-currently amended) The VLP of claim 1 or 2 wherein the L polypeptide comprises ~~an~~ the amino acid sequence substantially as set forth in SEQ ID NO: 7 or SEQ ID NO: 9 or a functional derivative thereof or comprises an amino acid sequence having at least ~~[[50%]]~~ 90% similarity-identity to SEQ ID NO: 7 or SEQ ID NO: 9.
7. (Withdrawn-currently amended) The VLP of claim 1 wherein the particle-associating portion of L polypeptide comprises ~~an~~ the amino acid sequence as set forth in SEQ ID NO:

7 or SEQ ID NO: 9 or a functional derivative thereof comprising an amino acid sequence having at least ~~[[50%]]~~90% similarity~~identity~~ to SEQ ID NO: 7 or SEQ ID NO: 9.

8. (Withdrawn-currently amended) The VLP of claim 1 or 2 wherein the particle-associating portion of L-polypeptide comprises or consists essentially of amino acids 24 to 107 of SEQ ID NO: 9 or an amino acid sequence having at least ~~[[50%]]~~90% similarity~~identity~~ thereto.
9. (Withdrawn) The VLP of claim 1 wherein the L polypeptide is a DHBV L polypeptide or functional derivative thereof.
10. (Withdrawn-currently amended) The VLP of claim 1 wherein said L polypeptide or particle-associating portion thereof is encoded by ~~a~~the sequence of nucleotides as set forth in SEQ ID NO: 6 or SEQ ID NO: 8 or having at least about ~~[[50%]]~~90% similarity~~identity~~ to SEQ ID NO: 6 or SEQ ID NO: 8 or a contiguous sequence of nucleotides capable of hybridizing to a complementary form of SEQ ID NO: 6 or SEQ ID NO: 8 under hybridisation conditions of medium stringency.
11. (Withdrawn) The VLP of claim 1 or 2 wherein the L polypeptide further comprises a signal sequence.
12. (Currently amended) A fusion ~~An isolated or recombinant~~ polypeptide for use in the assembly of a VLP comprising an avian hepadnavirus small envelope (S) polypeptide or a functional derivative thereof, said fusion polypeptide comprising a polypeptide of interest (POI) and at least a particle-associating portion of a large envelope polypeptide (L) of an avian hepadnavirus, ~~or a functional derivative thereof~~, wherein the POI is not a pre-S region of an avian hepadnavirus, wherein the POI is located (i) in the pre-S domain, (ii) N-terminally to the L polypeptide, (iii) at the amino terminal side of the S domain, or (iv) at the amino terminal side of the S domain minus the TM1 domain, and wherein the fusion polypeptide associates with said VLP comprising an avian hepadnavirus S polypeptide or a functional derivative thereof.

13. (Currently amended) ~~A recombinant polypeptide capable of assembling into a VLP when expressed in a cell, comprising a polypeptide of interest (POI) and at least a particle associating portion of a large envelope polypeptide (L) of an avian hepadnavirus or a functional derivative thereof, wherein the POI is not a pre-S region of an avian hepadnavirus.~~ A fusion polypeptide for use in the assembly of a VLP comprising an avian hepadnavirus small envelope (S) polypeptide or a functional derivative thereof, said fusion polypeptide comprising a polypeptide of interest (POI) and at least a particle-associating portion of a large envelope polypeptide (L) of an avian hepadnavirus wherein the POI is not a pre-S region of an avian hepadnavirus, and wherein the particle-associating portion comprises (i) the S domain of L, (ii) the L polypeptide minus the preS domain or minus the TM1 domain, (iii) the S domain minus the TM1 domain, or (iv) a portion of the L polypeptide which is downstream of TM1 and comprises at least TM2, the 5' cysteine loop between TM1 and TM2, and sequences downstream of TM2, wherein the fusion polypeptide associates with said VLP comprising an avian hepadnavirus small envelope (S) polypeptide or a functional derivative thereof.
14. (Currently amended) The polypeptide of claim 12 or 13 wherein the particle-associating portion of L ~~comprises at least~~ consists of (i) the S domain of L, (ii) the S domain of L absent minus the TM1 domain, or a functional derivative thereof or (iii) a portion of the L polypeptide which is downstream of TM1 and comprises at least TM2, the 5' cysteine loop between TM1 and TM2, and sequences downstream of TM2.
- 15 - 16. (Canceled)
17. (Currently amended) The polypeptide of claim 12 or 13 wherein the particle-associating portion of L polypeptide consists of ~~an the~~ the amino acid sequence as set forth in ~~SEQ ID NO: 7 or SEQ ID NO: 9 or a functional derivative thereof comprising or~~ amino acid sequence having at least ~~[[50%]]~~ 90% identity to ~~SEQ ID NO: 7 or SEQ ID NO: 9~~ (S domain of L).
18. (Currently amended) The polypeptide of claim 12 or 13 wherein the particle-associating

portion of L-polypeptide ~~comprises or~~ consists essentially of amino acids 24 to 107 of SEQ ID NO: 9 or an amino acid sequence having at least ~~[[50%]]~~90% identity thereto.

19. (Currently amended) The ~~recombinant or isolated~~ polypeptide of claim 12 or 13 wherein said ~~L-polypeptide or~~ particle-associating portion thereof is encoded by ~~[[a]]~~ the sequence of nucleotides as set forth in ~~SEQ ID NO: 6 or~~ SEQ ID NO: 8 or having at least about ~~[[50%]]~~90% identity to ~~SEQ ID NO: 6 or~~ SEQ ID NO: 8 or a contiguous sequence of nucleotides capable of hybridizing to a complementary form of ~~SEQ ID NO: 6 or~~ SEQ ID NO: 8 under hybridisation conditions of medium stringency.
20. (Previously presented) The polypeptide according to claim 12 or 13 wherein said L polypeptide further comprises a signal sequence.
21. (Currently amended) The polypeptide of claim 12 or 13 wherein the L polypeptide is a DHBV L polypeptide ~~or a functional derivative thereof~~.
22. (Withdrawn) A recombinant nucleic acid molecule for use in making a VLP, said nucleic acid molecule comprising a contiguous sequence of nucleotides encoding a fusion protein comprising a polypeptide of interest (POI) and at least a particle-associating portion of an L polypeptide of an avian hepadnavirus or a functional derivative thereof, wherein the POI is not a pre-S region of an avian hepadnavirus.
23. (Withdrawn) A recombinant nucleic acid molecule for use in making a VLP, said nucleic acid molecule comprising a contiguous sequence of nucleotides encoding i) a fusion polypeptide comprising a polypeptide of interest (POI) and at least a particle-associating portion of an L polypeptide of an avian hepadnavirus or a functional derivative thereof, and ii) a small envelope (S) polypeptide of an avian hepadnavirus or a functional derivative thereof, wherein the POI is not a pre-S region of an avian hepadnavirus.
24. (Withdrawn) The nucleic acid molecule of claim 22 or 23 wherein the particle-associating portion of L comprises at least the S domain of L, or the S domain of L minus the TM1 domain, or a functional derivative thereof.

25. (Withdrawn) The nucleic acid molecule of claim 22 or 23 wherein the POI is located in the pre-S domain of L or at the amino terminal side of the S domain of L, or the S domain minus the TM1 domain of L.
26. (Withdrawn-currently amended) The nucleic acid molecule of claim 22 or 23 which encodes an L polypeptide comprising an amino acid sequence substantially as set forth in SEQ ID NO: 7 or SEQ ID NO: 9 or comprises an amino acid sequence having at least ~~[[50%]]~~90% identity to SEQ ID NO: 7 or SEQ ID NO: 9.
27. (Withdrawn-currently amended) The nucleic acid molecule of claim 26 which encodes a particle associating portion of L polypeptide consisting essentially of amino acids 24 to 167 of SEQ ID NO: 9 or an amino acid sequence having at least ~~[[50%]]~~90% identity to SEQ ID NO: 9.
28. (Withdrawn-currently amended) The nucleic acid molecule of claim 22 or 23 wherein said L polypeptide or particle associating portion thereof is encoded by a sequence of nucleotides as set forth in SEQ ID NO: 6 or SEQ ID NO: 8 or having at least about ~~[[50%]]~~90% identity to SEQ ID NO: 6 or SEQ ID NO: 8 or a contiguous sequence of nucleotides capable of hybridizing to a complementary form of SEQ ID NO: 6 or SEQ ID NO: 8 under hybridisation conditions of medium stringency.
29. (Withdrawn) The nucleic acid molecule of claim 22 or 23 wherein the L polypeptide further comprises a signal sequence.
30. (Withdrawn) The nucleic acid molecule of claim 22 or 23 wherein the L polypeptide is a DHBV L polypeptide or functional derivative thereof.
- 31-39. (Canceled)
40. (Withdrawn) An isolated and/or recombinant cell comprising the nucleic acid molecule of any one of claims 22 to 30 or expressing the polypeptide of any one of claims 12 to 21 or the

VLP of any one of claims 1 to 11.

41. (Withdrawn) The cell according to claim 40 wherein said cell is a eukaryotic cell, preferably a yeast, avian or mammalian cell.
42. (Withdrawn) A method of delivering a POI to a subject or cell comprising expressing the POI in a VLP comprising L polypeptide from an avian hepadnavirus or a functional derivative thereof such that at least part of the POI is expressed on the surface of the VLP and administering the VLP to a subject or cell.
43. (Withdrawn) The method of claim 42 wherein the VLP is made in an *in vitro* expression system such as a yeast, avian or mammalian expression system.
44. (Withdrawn) The method of claim 42 wherein the VLP is made *in vivo* in the cells of a subject after administration of the nucleic acid molecule of any one of claims 22 to 30.
45. (Withdrawn) A method for making a recombinant VLP said method comprising:
 - i) cloning a nucleic acid molecule encoding a polypeptide of interest into an expression vector comprising a particle-associating portion of an L polypeptide of an avian hepadnavirus, such as DHBV, or a functional derivative thereof;
 - ii) introducing the recombinant expression vector of step i) into a suitable cell and maintaining same under conditions which allow protein expression and particle assembly with S polypeptide of an avian hepadnavirus, such as DHBV, or a functional derivative thereof; and
 - iii) recovering said virus-like particles from said cells.
46. (New) The fusion polypeptide of claim 13, wherein the particle-associating portion comprises TM2.
47. (New) The fusion polypeptide of claim 13, wherein the particle-associating portion

comprises TM2 and the cysteine loop between TM1 and TM2, and optionally, an additional amino acid sequence downstream of TM2.